REMARKS

Claims 17, 20-27, 29-31 and 33-42 are pending in the present application. Claims 17, 20-27, 29-31 and 33 are rejected. Claims 17 and 21 are herein amended. Claim 23 is herein cancelled without prejudice.

Applicants' Response to Claim Rejections under 35 U.S.C. §112

Claims 17, 20-22, 24-27, 29, 30-31 and 33 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is the position of the Office Action that these claims are indefinite because independent claims 17 and 21, which recite the limitation "...expressed by– $(O - R_1)_n$ –,..." do not define the variable "n". The Office Action suggests amending the claims to recite what "n" represents. Accordingly, Applicants herein amend claims 17 and 21 in order to incorporate the subject matter of claim 23, which recites that "n is an integer number in the range of 4 to 450." Likewise, Applicants herein cancel claim 23. Applicants respectfully submit that this amendment does not raise new issues requiring further search or consideration. Favorable reconsideration is respectfully requested.

Applicants' Response to Claim Rejections under 35 U.S.C. §103

Claims 17, 21-24, 26, 27, 29 and 30 were rejected under 35 U.S.C. §103(a) as being unpatentable over Corn et al. (U.S. Patent No. 6,127,129) in view of Fodor et al. (U.S. Patent No. 5,424,186), as evidenced by Sato et al. (U.S. Patent No. 5,997,958).

It is the position of the Office Action that Corn discloses the invention as claimed, with the exception of teaching "a heterobifunctional linker wherein the X group and the Y group are linked with a polyethylene glycol portion." The Office Action relies on Fodor to provide this teaching. Applicants note that this is not the actual claim language recited by independent claims 17 and 21. Rather, this is one embodiment encompassed by the independent claims.

It is additionally noted that previous Office Actions proposed a modification of Corn such that a portion of the linker of Corn was replaced by the linker of Fodor. However, the pending Office Action now proposes modifying Corn by substituting the entire linker of Fodor for the linker of Corn. The Office Action confirms this on page 8 of the pending Office Action, stating "the examiner is replacing the entire SSMCC linker of Corn et al with the hydrophilic linker of Fodor et al."

Corn is directed at a process to create biomolecule and/or cellular arrays on metal surfaces. Corn discloses a fabrication scheme for a biochip, where a PEG background surrounds a plurality of DNA attachment sites. As illustrated in Figure 4, a gold (Au) substrate is attached to a DNA via 11-mercaptoundecylamine (MUAM) and sulfosuccinimidyl 4-(N-maleimidomethyl)cyclohexane-1-carboxylate (SSMCC).

Applicants respectfully submit that the pending Office Action mischaracterizes the linker of Corn. On page 4 of the pending Office Action, it is alleged that Corn discloses:

> a heterobifunctional polymer molecule in the form of a hydrophilic polymer MUAM (column 7, lines 53-54), which has a mercapto group covalently bound to a surface of a solid surface (i.e., X; column 3, lines 58-59) and an amino group (i.e., Y) which attaches to the DNA (step 5 of Figure 4).

However, the MUAM is only a portion of the linker of Corn. The amino group illustrated in Step 5 of Figure 4 does not bind to the DNA. Rather, the amino group binds to SSMCC, which binds to thiol-modified DNA. See column 8, line 65 to column 9, line 18.

Fodor does not disclose the claimed linker

Fodor is directed at a very large scale immobilized polymer synthesis. On page 5 of the Office Action, the Office Action alleges that Fodor teaches immobilizing an oligonucleotide using:

> a heterobifunctional linker having a functional group X in the form on an amine and a functional group Y in the form of a carboxyl group which is derived from photocleavage of the molecule NVOC, and a hydrophilic repeating polymer in the form of ethylene glycol oligomers.

The Office Action cites column 14, lines 28-45 and column 3, line 52 to column 4, line 5 to support this position.

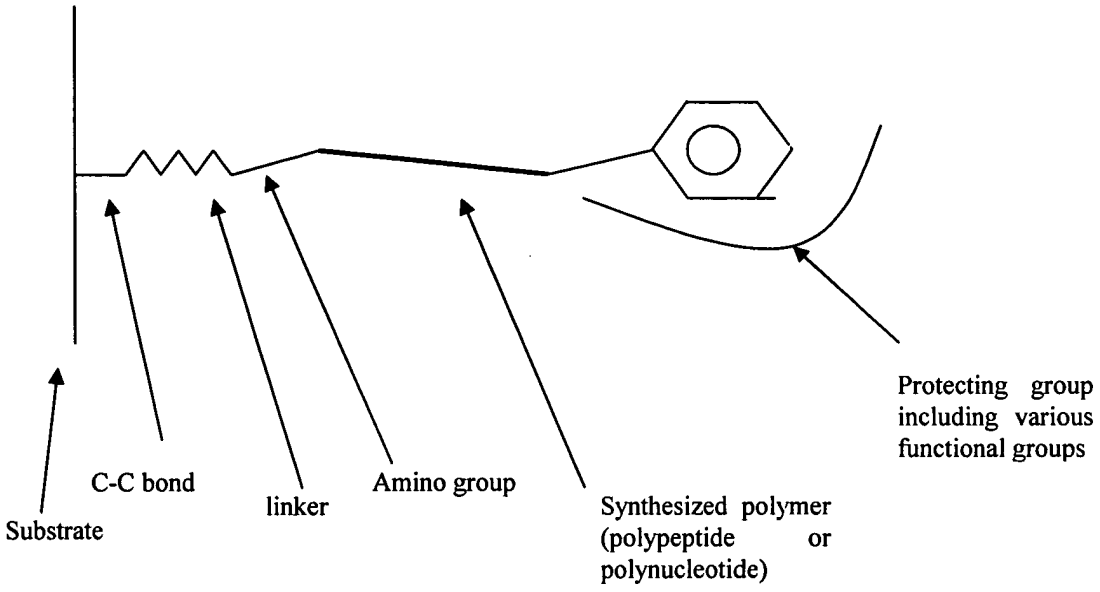
However, Fodor does not actually disclose this. Fodor discloses synthesizing polymers on a substrate. As illustrated in Figure 1, a linker ("zig-zag" line) is attached to a solid support 2. Initially, an amino group (NH) is disposed at the terminal end of the linker and is bonded to a protecting group (X). In order to synthesize a polymer, the protecting group X is removed by

photo-deprotection. Then, a monomer (A) bound to another protecting group (X) is bound to the unprotected amino group (NH). This step may be repeated many times until a polymer is synthesized on the substrate. See column 13, line 66 to column 14, line 15.

The Office Action points to column 3, line 52 to column 4, line 5 to support the pending rejection. This passage mentions R-groups including an amino and carboxyl group. However, it is important to note that these are merely R groups of a protecting group illustrated between lines 55 and 64 of column 3. These groups are not bound to the terminal ends of the linker molecule, as alleged by the Office Action. One end of the protecting group is bound to "Y," which is "an oxygen of the carboxyl group of a natural or unnatural amino acid, an amino group of a natural or unnatural amino acid, or the C-5' oxygen group of a natural or unnatural deoxyribonucleic or ribonucleic acid." The other end of the protecting group remains free. Thus, these R groups are not bound to the terminal ends of the linker, but are bound to the free end of the protecting group.

Additionally, the Office Action points to column 14, lines 28-45, apparently relying on the statement that "[w]hen a polymer sequence to be synthesized is, for example, a polypeptide, amino groups at the ends of the linkers attached to a glass substrate are derivatized with..." However, based on the totality of the reference, it is clear that the amino group referred to is not bound to the substrate, but rather is on the end of the linker opposite from the substrate, interposing the linker and the polymer. As disclosed at column 15, line 67 to column 16, line 2, the linker is attached to the substrate by "carbon-carbon bonds." The linker molecules should be 6-50 atoms long and can be ethylene glycol oligomer containing 2-10 monomer units.

Thus, Fodor discloses the arrangement described in the following crude illustration:



This configuration is confirmed by the passage at column 12, lines 1 to 41, which discloses a substrate-linker-polymer(comprised of multiple monomers)-protecting group arrangement. Accordingly, Applicants respectfully submit that Fodor does not disclose or suggest the linker as claimed. The linker of Fodor is not heterobifunctional as recited by claims 17 and 21. In fact, the linker only has one functional group, on the side which is opposite from the substrate. Thus, the linker is actually monofunctional. Thus, Fodor does not disclose or suggest the claimed linker. Since Fodor does not disclose the claimed linker, the combination of Corn and Fodor does not disclose or suggest the invention as claimed. Accordingly, Applicants respectfully traverse the rejection.

Alleged inaccuracies in the Table on page 14 of the previously filed amendment

With respect to the summary table on page 14 of the amendment filed on October 3, 2007, the Office Action states that this table contains several inaccuracies. See section "B" of the Office Action on pages 8 and 9. The Office Action states that the first inaccuracy is that the heterobifunctionality of the linker of Fodor is not disclosed. The Office Action again alleges that Fodor discloses an amine on one end and a carboxyl group on the other end, citing column 14, lines 28-45 and column 3, line 52 to column 4, line 5. As explained above, the linker of Fodor is directly attached to the substrate, and has an amine group on the end opposite the substrate. Thus, the linker of Fodor only has one functional group. As such, the linker cannot be heterobifunctional. Instead, it is merely a monofunctional linker.

The Office Action states that the second inaccuracy is that the X group bound to the solid surface is not disclosed. The Office Action points to column 14, lines 28-46 to allege that the linker is bound to the substrate by an amino group. As discussed above, this amino group is on the side of the linker opposite the substrate. The linker is actually bound to the substrate directly, via a carbon-carbon bond. See Figure 1 and column 15, line 67 to column 16, line 2.

The Office Action states that the third inaccuracy is that the Y group bound to the oligonucleotide is not disclosed. The Office Action alleges that this carboxyl group is bound to the linker and the oligonucleotide chain. However, as discussed above, the carboxyl group to which the Office Action refers is actually a functional group on the protecting group, not the linker.

Unexpected results

Next, Applicants discuss the first section "D" of the Office Action on pages 9 and 10.[1] In this passage, the Office Action states that the unexpected results illustrated by Kyo are not commensurate in scope with the claims. According to MPEP §716.02(d), any teaching of unexpected results must be commensurate in scope with the claims. In other words, because the NHS-PEG-MAL linker tested in Kyo is only one of many linkers covered by the present claims, it is not entirely clear that these unexpected results would be exhibited over the entire range of possible linkers encompassed by the claims.

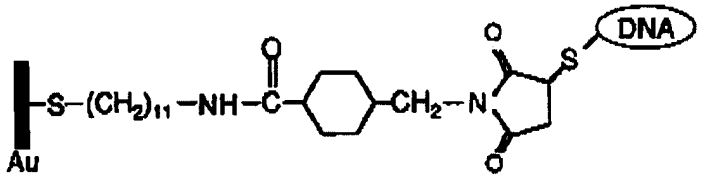
However, the nonobviousness of a broader claimed range can be supported by evidence based on unexpected results from testing a narrower range if one of ordinary skill in the art would be able to determine a trend in the exemplified data which would allow the artisan to reasonably extend the probative value thereof. *In re Kollman*, 595 F.2d 48, 201 USPQ 193 (CCPA 1979). Applicants respectfully submit that it is not only the linker of Kyo that shows unexpected results, but rather a larger range of linkers.

Additionally, the Office Action states that Kyo does not compare the NHS-PEG-MAL linker against the appropriate linker. The Office Action states that Kyo compares the NHS-PEG-MAL linker with the linker SSMCC. The Office Action is correct in stating that the linker of Corn is MUAM covalently linked to SSMCC. However, the descriptors "SSMCC" and "NHS-

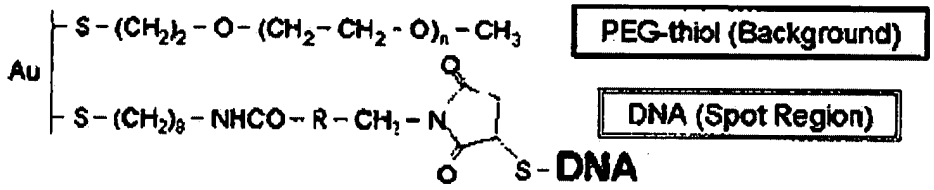
[1] Applicants note that the Office Action appears to contain an error in that there are two sections of the Office Action labeled "D".

PEG-MAL" only describe the "heart" of the linker, while not describing the portion of the linker which links SSMCC or NHS-PEG-MAL to the substrate.

Accordingly, Applicants clarify that, as illustrated in Figure 4, the linker of Corn is:



Furthermore, as illustrated in Figure 2 of Kyo, the linker of Kyo is:



R may have a value of:

Thus, the only difference between the linker of Kyo and the linker of Corn is that in Kyo, the linker includes $-(CH_2)_8-$, while in Corn, the linker includes $-(CH_2)_{11}-$. The linkers of Kyo and Corn are otherwise identical. Applicants note that this difference does not affect the characteristics of the linker. Thus, the comparison is appropriate.

Hydrophobic vs. hydrophilic

Finally, Applicants discuss the second section "D", on page 10 of the Office Action. In this section, the Office Action comments on Applicants' remarks that the combination of Corn and Fodor is "fatal" because one linker is hydrophobic and one is hydrophilic. The Office Action

points to column 3, lines 15-22 to argue that the areas where the nucleic acid is not located (i.e., the background) is hydrophobic. To be more accurate, this passages states that the background must be "sufficiently hydrophobic so as to allow "pinning" of aqueous solutions of biomolecules or cells at specific array locations." Since the Office Action concludes that the background is hydrophobic, the Office Action concludes that the nucleic acid attachment points are hydrophilic.

The Office Action goes on to state that after the nucleic acids have been attached, the background area is converted to a hydrophilic area. The linker of Corn is mostly hydrophobic, with the exception of the thiol, attached to the DNA, which is hydrophilic. Thus, the Office Action's conclusion that the nucleic acid attachment area is hydrophilic is inaccurate. Accordingly, Corn discloses a hydrophobic area in which DNA is attached, and a background which is hydrophilic.

Furthermore, the Office Action alleges that Drumheller (discussed below) teaches that a hydrophilic DNA attachment area and a hydrophilic background area are compatible. However, Drumheller discusses a background area.

With respect to the advantages of having both a hydrophilic background and a hydrophilic DNA attachment area, Applicants provide the following comments. In the case of a hydrophilic background, excellent effects of inhibiting non-specific adsorption are achieved. Further, a large contrast is provided relative to the spot area. See paragraphs [0085] and [0086] of the pending application. Further, in the case of a hydrophilic attachment area, the immobilized biomolecule has excellent mobility. See paragraphs [0113], [0115] and [0092] of the pending application.

In Kyo, Figure 3A represents a hydrophilic background and a hydrophobic attachment area. This the same configuration as that disclosed by Corn. On the other hand, Figure 3B represents a hydrophilic background and a hydrophilic attachment area. Clearly, in Figure 3B, a robust increase of SPR signal was observed for MARE25 on the NHS-PEG-MAL immobilized array. On the contrary, the increase in SPR signal was not observed for MARE25 on the SSMCC-immobilized array (Figure 3A). This evidence illustrates that hydrophilic NHS-PEG-MAL (MW 3400) is important for measuring of the interaction between a first biomolecule and a second biomolecule.

Accordingly, for at least the above reasons, Applicants respectfully submit that the pending rejection is improper. Favorable reconsideration is respectfully requested.

Claim 25 was rejected under 35 U.S.C. §103(a) as being unpatentable over Corn in view of Fodor, as evidenced by Sato, and in further view of Drumheller (U.S. Patent No. 6,874,165).

It is the position of the Office Action that the combination of Corn and Fodor, as evidenced by Sato, discloses the invention as claimed, with the exception of a compound having the formula of X'-R'-Y' between the gold layer and the other heterobifuncational hydrophilic polymer (X-R-Y). The Office Action relies on Drumheller to provide this teaching. First, Applicants respectfully submit that claim 25 is patentable at least due to its dependency on claim 21, which Applicants submit is patentable for at least the reasons discussed above.

Drumheller is directed at materials and methods for the immobilization of bioactive species onto polymeric substrates. As illustrated in Figure 8, Drumheller discloses a support member 82 having a first layer 84 and a second layer 86 disposed thereon. The first layer may be polyethylene glycol. See column 11, line 61. The second layer may also be polyethylene glycol. See column 14, line 56. Between the first layer 84 and the second layer 86 is a functional group A. Between the second layer 86 and the bioactive species B is a functional group Z. Drumheller discloses that these functional groups may be one of many different groups. See column 15, lines 16-40.

The Office Action alleges that the first layer 84 "has two functional groups," citing column 10, line 60 to column 11, line 14. This passage states that:

> Preferred copolymers for formation of the first layer are copolymers comprised at least one moiety capable of physicochemically adsorbing to the support member, a moiety capable of chemical modification with a suitable agent, and a moiety capable of interacting with high surface tension fluids. These moieties may be selected such that one moiety fulfills all of these three roles simultaneously, fulfills two roles, or fulfills only one role.

This passage does not disclose that a functional group interposes the support and the first layer. Instead, the first layer attaches to the support member by "physicochemical adsorption." See column 10, line 67 to column 11, line 5. Drumheller only discloses a configuration of substrate--first layer (e.g., polyethylene glycol)--functional group--second layer (e.g., polyethylene glycol)--functional group--biomolecule. Accordingly, the combination of Corn, Fodor and Drumheller does not disclose the invention as claimed. Favorable reconsideration is respectfully requested.

Claims 20 and 33 were rejected under 35 U.S.C. §103(a) as being unpatentable over Corn in view of Fodor, as evidenced by Sato, and in further view of Noblett (U.S. Patent No. 6,362,004).

It is the position of the Office Action that the combination of Corn and Fodor, as evidenced by Sato discloses the invention as claimed, with the exception of markers on the array indicative of spots. The Office Action relies on Noblett to provide this teaching. In response, Applicants respectfully submit that claims 20 and 33 are patentable due to their dependency on claims 17 and 21, which Applicants submit are patentable for at least the reasons discussed above. Favorable reconsideration is respectfully requested.

Claim 31 was rejected under 35 U.S.C. §103(a) as being unpatentable over Corn in view of Fodor, as evidenced by Sato, and in further view of Wiegel (U.S. Patent No. 6,107,034).

It is the position of the Office Action that the combination of Corn and Fodor, as evidenced by Sato discloses the invention as claimed, with the exception of transfer factors. The Office Action relies on Wiegel to provide this teaching. In response, Applicants respectfully submit that claim 31 is patentable due to its dependency on claim 21, which Applicants submit is patentable for at least the reasons discussed above. Favorable reconsideration is respectfully requested.

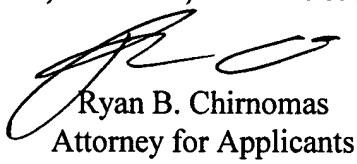
For at least the foregoing reasons, the claimed invention distinguishes over the cited art and defines patentable subject matter. Favorable reconsideration is earnestly solicited.

Should the Examiner deem that any further action by applicants would be desirable to place the application in condition for allowance, the Examiner is encouraged to telephone applicants' undersigned attorney.

If this paper is not timely filed, Applicants respectfully petition for an appropriate extension of time. The fees for such an extension or any other fees that may be due with respect to this paper may be charged to Deposit Account No. 50-2866.

Respectfully submitted,

WESTERMAN, HATTORI, DANIELS & ADRIAN, LLP



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